#### GSK-3B Sequence

Met 1	Ser	Gly	Arg	Pro 5	_	Thr <sub>.</sub>	Thr	Ser	Phe 1		Glu	Ser	Cys	Lys 1	_
Val	Gln	G1n 2		Ser	Ala	Phe	· ·	Ser 5	Met	Lys	Val	Ser 3		Asp	Lys
Asp	Gly	Ser 3!	_	Val	Thr	Thr	Va1 4		Ala	Thr	Pro	Gly 4		Gly	Pro
Asp	Arg	Pro 5		Glu	Val	Ser		Thr 5	Asp	Thr	Lys	Val 6		Gly	Asn
G1y 65	Ser	Phe	Gly	Val	Va1 70	Tyr	Gln	Ala	Lys	Leu 75	Cys	Asp	Ser	Gly	Glu 80
Leu	Val	Ala 8		Lys	Lys	Val		G1n O	Asp	Lys	Arg	Phe 9		Asn	Arg
Glu	Leu	Gln 10		Met	Arg	Lys		Asp 05	His	Cys	Asn		Va1 10	Arg	Leu
Arg	Tyr	Phe 11		Tyr	Ser	Ser	-	G1u 20	Lys	Lys	<b>A</b> sp		Va1 25	Tyr	Leu
Asn	Leu	Val 13		Asp	Tyr	Val		Glu 35	Thr	Val	Tyr	-	Va1 40	Ala	Arg
His 145	Tyr	Ser	Arg	Ala	Lys 150	Gln	Thr	Leu	Pro	Va1 155	Ile	Tyr	Val	Lys	Leu 160
Tyr	Met	Tyr 16		Leu	Phe	Arg		Leu 70	Ala	Tyr	Ile		Ser 75	Phe	Gly
Ile	Cys	His 18	-	Asp	Ile	Lys		G1n 85	Asn	Leu	Leu		Asp 90	Pro	Asp
Thr	A1a	Va1 19		Lys	Leu	Cys		Phe 00	Gly	Ser	Ala	•	G1n 05	Leu	Val

Arg	Gly 210	Glu	Pro	Asn	Val	Ser 215	Tyr	Ile	Cys	Ser	Arg 220	Tyr	Tyr	Arg	Ala
Pro 225	Glu	Leu	Ile	Phe	G1y 230	Ala	Thr	Asp	Tyr	Thr 235	Ser	Ser	Ile	Asp	Va1 · 240
Trp	Ser	Ala	G1y	Cys 245	Val	Leu	Ala	Glu	Leu 250	Leu	Leu	Ġly	Gln	Pro 255	Ile
Phe	Pro	Gly	Asp 260	Ser	Gly	Val	Asp	G1n 265		Val	Glu	Ile	Ile 270	Lys	Va1 _
Leu	Gly	Thr 275	Pro	Thr	Arg	G1u	G1n 280	Ile	Arg	Glu	Met	Asn 285	Pro	Asn	Tyr
Thr	G1u 290	Phe	Lys	Phe	Prọ	G1n 295	Ile	Lys	Ala	His	Pro 300	Trp	Thr	Lys	Val
Phe 305	Arg	Pro	Arg	Thr	Pro 310	Pro	Glu	Ala	Ile	A1a 315		Cys	Ser	Arg	Leu 320
Leu	Glu	Tyr	Thr	Pro 325	Thr	Ala	Arg	Leu	Thr 330	Pro	Leu	Glu	Ala	Cys 335	Ala
His	Ser	Phe	Phe 340	Asp	Glu	Leu	Arg	Asp 345	Pro	Asn	Val	Lys	His 350	Pro	Asn
Gly	Arg	Asp 355	Thr	Pro	Ala	Leu	Phe 360	Asn	Phe	Thr	Thr	G1n 365	Glu	Leu	Ser
Ser	Asn 370	Pro	Pro	Leu	Ala	Thr 375	Ile	Leu	Ile	Pro	Pro 380	His	Ala	Arg	Ile
61n 385	Ala	Ala	Ala	Ser	Thr 390	Pro	Thr	Asn	Ala	Thr 395		Ala	Ser	Asp	Ala 400
Asn	Thr	Gly	Asp	Arg 405	Gly	Gln	Thr	Asn	Asn 410	Ala	Ala	Ser	Ala	Ser 415	Ala
Ser	Asn	Ser	Thr 420		÷			•		_					

Fig. 1B

### GSK-3 $\beta$ 557 Construct Sequence Met Glu Tyr Met Pro Met Glu Gly Gly Gly

Val Gln Gln Pro Ser Ala Phe Gly Ser Met Lys Val Ser Arg Asp 20 25 30  Asp Gly Ser Lys Val Thr Thr Val Val Ala Thr Pro Gly Gln Gly 40 45  Asp Arg Pro Gln Glu Val Ser Tyr Thr Asp Thr Lys Val Ile Gly 50 55 60  Gly Ser Phe Gly Val Val Tyr Gln Ala Lys Leu Cys Asp Ser Gly 70 75  Leu Val Ala Ile Lys Lys Val Leu Gln Asp Lys Arg Phe Lys Asn 85 90 95  Glu Leu Gln Ile Met Arg Lys Leu Asp His Cys Asn Ile Val Arg 100 105 110  Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115 120 125  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe 165 170 175	Pro 5
Asp Arg Pro Gln Glu Val Ser Tyr Thr Asp Thr Lys Val Ile Gly 50 55 60  Gly Ser Phe Gly Val Val Tyr Gln Ala Lys Leu Cys Asp Ser Gly 65 70 75  Leu Val Ala Ile Lys Lys Val Leu Gln Asp Lys Arg Phe Lys Asn 85 90 95  Glu Leu Gln Ile Met Arg Lys Leu Asp His Cys Asn Ile Val Arg 100 105 110  Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115 120 125  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Lys
Gly Ser Phe Gly Val Val Tyr Gln Ala Lys Leu Cys Asp Ser Gly 70 75  Leu Val Ala Ile Lys Lys Val Leu Gln Asp Lys Arg Phe Lys Asn 85 90 95  Glu Leu Gln Ile Met Arg Lys Leu Asp His Cys Asn Ile Val Arg 100 105 110  Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115 120 125  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Pro
Leu Val Ala Ile Lys Lys Val Leu Gln Asp Lys Arg Phe Lys Asn 85 90 95  Glu Leu Gln Ile Met Arg Lys Leu Asp His Cys Asn Ile Val Arg 100 105 110  Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115 120 125  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Asn
Glu Leu Gln Ile Met Arg Lys Leu Asp His Cys Asn Ile Val Arg 100  Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Glu 80
Arg Tyr Phe Phe Tyr Ser Ser Gly Glu Lys Lys Asp Glu Val Tyr 115 120 125  Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Arg
Asn Leu Val Leu Asp Tyr Val Pro Glu Thr Val Tyr Arg Val Ala 130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Leu
130 135 140  His Tyr Ser Arg Ala Lys Gln Thr Leu Pro Val Ile Tyr Val Lys 145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Leu
145 150 155  Tyr Met Tyr Gln Leu Phe Arg Ser Leu Ala Tyr Ile His Ser Phe	Arg
· · · · · · · · · · · · · · · · · · ·	Leu 160
	Gly
Ile Cys His Arg Asp Ile Lys Pro Gln Asn Leu Leu Leu Asp Pro 180 185 190	Asp
Thr Ala Val Leu Lys Leu Cys Asp Phe Gly Ser Ala Lys Gln Leu 195 200 205	Val
Arg Gly Glu Pro Asn Val Ser Tyr Ile Cys Ser Arg Tyr Tyr Arg 210 215 220	43:

Fig. 2A

Pro Glu Leu Il 225	e Phe Gly Ala 230	• •	Thr Ser Ser Ile 235	Asp Val 240
Trp Ser Ala Gl	y Cys Val Leu 245	ı Ala Glu Leu l 250	Leu Leu Gly Gln	Pro Ile 255
Phe Pro Gly As		Asp G1n Leu \ 265	Val Glu Ile Ile 270	Lys Val
Leu Gly Thr Pr 275	o Thr Arg Glu	Gln Ile Arg ( 280	Glu Met Asn Pro 285	Asn Tyr
Thr Glu Phe Ly 290	s Phe Pro Gln 295	•	His Pro Trp Thr 300	Lys Val
Phe Arg Pro Ar 305	g Thr Pro Pro 310		Ala Leu Cys Ser 315	Arg Leu 320
Leu Glu Tyr Th	r Pro Thr Ala 325	Arg Leu Thr F	Pro Leu Glu Ala	Cys Ala 335
His Ser Phe Ph 34	•	Arg Asp Pro <i>I</i> 345	Asn Val Lys His 350	Pro Asn
Gly Arg Asp Th 355	r Pro Ala Leu	Phe Asn Phe 1 360	Thr Thr G1n G1u 365	Leu Ser
Ser Asn Pro Pr 370	o Leu Ala Thr 375		Pro Pro His Ala 380	Arg Ile

### GSK-3ß 580 Construct Sequence Het Glu Tyr Het Pro Het Glu Gly Gly Gly

G	y Se	er Lys Va 35	al Th	ir Th	ır Va	11 Val 40	Ala Th	ar Pr	o G1	y G1 4!		y Pr	0
<b>\</b> sp	Arg	Pro G1n 50	Glu	Val	Ser	Tyr Th	r Asp	Thr	Lys	Va1 61		Gly	Asn
31y 65	Ser	Phe Gly	Val	Va1 70	Tyr	GIn Al	a Lys	Leu 75	Cys.	Asp	Ser	Gly	Glu 80
_eu	Val	Ala Ile 85	Lys	Lys	Val	Leu Gl 90	n Asp	Lys	Arg		Lys 5	Asn	Arg
alu	Leu	Gln Ile 100	Met	Arg	Lys	Leu As 105	p His	Cys	Asn	Ile 11		Arg	Leu
\rg	Tyr	Phe Phe 115	Tyr	Ser	Ser	Gly Gl 120	u Lys	Lys	Asp	Glu 12		Tyr	Leu
<b>A</b> sn	Leu	Val Leu 130	Asp	Tyr	Val	Pro 61 135	u Thr	Val	Tyr	Arg 14		Ala	Arg
tis 145	Tyr	Ser Arg	Ala	Lys 150	Gln	Thr Le	u Pro	Va1 155	Ile	Tyr	Val	Lys	Leu 160
Гуг	Met	Tyr Gln 165	Leu	Phe	Arg	Ser Le 170	u Ala	Tyr	Ile	His 17		Phe	Gly
Ile	Cys	His Arg 180	Asp	Ile	Lys	Pro G1 185	n Asn	Leu	Leu	Leu 19	•	Pro	Asp
Thr	Ala	Val Leu 195	Lys	Leu	Cys	Asp Ph 200	e Gly	Ser	Ala	Lys 20		Leu	Val
Arg	Gly	Glu Pro 210	Asn	Val	Ser	Tyr Il 215	e Cys	Ser	Arg	Tyr 22		Arg	Ala
Pro 225		Leu Ile	Phe	G1y 230	Ala	Thr As	p Tyr	Thr 235	Ser	Ser	Ile	Asp	Va1 240

Trp Ser Ala Gly	Cys Val Leu Al	la Glu Leu Leu Leu	Gly Gln Pro Ile
	245	250	255
Phe Pro Gly Asp	Ser Gly Val As	sp Gln Leu Val Glu	Ile Ile Lys Val
260		265	270
Leu Gly Thr Pro	-	In Ile Arg Glu Met	Asn Pro Asn Tyr
275		30	285
Thr Glu Phe Lys 290	Phe Pro Gln I	le Lys Ala His Pro 300	Trp Thr Lys Val
Phe Arg Pro Arg	Thr Pro Pro Gi	lu Ala Ile Ala Leu	Cys Ser Arg Leu
305	310	315	320
Leu Glu Tyr Thr	Pro Thr Ala Ai	rg Leu Thr Pro Leu	Glu Ala Cys Ala
	325	330	335
His Ser Phe Phe 340	Asp Glu Leu Ai	rg Asp Pro Asn Val 345	Lys His Pro Asn 350
Gly Arg Asp Thr	Pro Ala Leu Pl	ne Asn Phe Thr Thr	Gln Glu Leu Ser
355	30	50	365
Ser Asn Pro Pro 370	Leu Ala Thr Il	le Leu Ile Pro Pro 380	His Ala Arg Ile

#### Human GSK $3\alpha$

MSGGGPSGGG	<b>PGGSGRARTS</b>	SFAEPGGGG	GGGGGPGGSA	SGPGGTGGGK
1				50
<b>ASVGAMGGGV</b>	GASSSGGGPG	GSGGGGGGP	GAGTSFPPPG	VKLGRDSGKV
51				100
TTVVATLGQG	PERSQEVAYT	DIKVIGNGSF	GVVYQARLAE	TRELVAIKKV
101				150
LQDKRFKNRE	LQIMRKLDHC	NIVRLRYFFY	SSGEKKDELY	LNLVLEYVPE
151				200
TVYRVARHFT	KAKLTIPILY	VKVYMYQLFR	SLAYIHSQGV	CHRDIKPONL
201				250
LVDPDTAVLK	LCDFGSAKQL	VRGEPNVSYI	CSRYYRAPEL	IFGATDYTSS
251				300
IDVWSAGCVL	AELLLGQPIF	PGDSGVDQLV	ELIKYLGTPT	REQIREMNPN
301		-		350
YTEFKFPQIK	<b>AHPWTKVFKS</b>	RTPPEAIALC	SSLLEYTPSS	RLSPLEACAH
351	2	*		400
SFFDELRCLG	TQLPNNRPLP	PLFNFSAGEL	SIQPSLNAIL	IPPHLRSPAG -
401				450
TTTLTPSSQA	LTETPTSSDW	<b>QSTDATPTLT</b>	NSS	
451			483	

### Human GSK $3\alpha$

MSGGGPSGGG	<b>PGGSGRARTS</b>	SFAEPGGGGG	<b>GGGGGPGGSA</b>	SGPGGTGGGK
1				50
<b>ASVGAMGGGV</b>	GASSSGGGPG	GSGGGGSGGP	GAGTSFPPPG	VKLGRDSGKV
51				100
TTVVATLGQG	PERSQEVAYT	DIKVIGNGSF	GVVYQARLAE	TRELVAIKKV
101				150
LQDKRFKNRE	LQIMRKLDHC	NIVRLRYFFY	SSGEKKDELY	LNLVLEYVPE
151				200
TVYRVARHFT	KAKLTIPILY	VKVYMYQLFR	SLAYIHSQGV	CHRDIKPONL
201				250
LVDPDTAVLK	LCDFGSAKQL	VRGEPNVSYI	CSRYYRAPEL	IFGATDYTSS
251				300
IDVWSAGCVL	AELLLGQPIF	PGDSGVDQLV	EIIKVLGTPT	REQIREMNPN
301				350
YTEFKFPQIK	AHPWTKVFKS	RTPPEAIALC	SSLLEYTPSS	RLSPLEACAH
351				400
SFFDELRCLG	TQLPNNRPLP	PLFNFSAGEL	SIQPSLNAIL	IPPHLRS
401				

#### Human GSK3a

			•	SGKV
				100
TTVVATLGQG	PERSQEVAYT	DIKVIGNGSF	GVVYQARLAE	TRELVAIKKY
101				150
LQDKRFKNRE	LQIMRKLDHC	NIVRLRYFFY	SSGEKKDELY	LNLVLEYVPE
151				200
TVYRVARHFT	KAKLTIPILY	VKVYMYQLFR	SLAYIHSQGV	CHRDIKPONL
201				250
LVDPDTAVLK	LCDFGSAKQL	VRGEPNVSYI	CSRYYRAPEL	<b>IFGATDYTSS</b>
251				300
IDVWSAGCVL	AELLLGQPIF	PGDSGVDQLV	EIIKVLGTPT	REQIREMNPN
301		•		350
YTEFKFPQIK	AHPWTKVFKS	RTPPEAIALC	SSLLEYTPSS	RLSPLEACAH
351				400
SFFDELRCLG	TQLPNNRPLP.	PLFNFSAGEL	SIQPSLNAIL	IPPHLRSPAG
401	•			450
TTTLTPSSQA	LTETPTSSDW	QSTDATPTLT	NSS	
451			483	

### Human GSK3 $\alpha$

				SGKV
				100
TTVVATLGQG	PERSQEVAYT	DIKVIGNGSF	GVVYQARLAE	TRELVAIKKY
101				150
LQDKRFKNRE	LQIMRKLDHC	NIVRLRYFFY	SSGEKKDELY	LNLVLEYVPE
151	•			200
TVYRVARHFT	KAKLTIPILY	VKVYMYQLFR	SLAYIHSQGV	CHRDIKPQNL
201				250
LVDPDTAVLK	LCDFGSAKQL	VRGEPNVSYI	CSRYYRAPEL	IFGATDYTSS
251				300
IDVWSAGCVL	AELLLGQPIF	PGDSGVDQLV	EIIKVLGTPT	REQIREMNPN
301		_		350
YTEFKFPQIK	AHPWTKVFKS	RTPPEAIALC	SSLLEYTPSS	RLSPLEACAH
351				400
SFFDELRCLG	TQLPNNRPLP	PLFNFSAGEL	SIQPSLNAIL	IPPHLRS
401				